

CLAIMS

1. – 52. (CANCEL)

53. (NEW) A method of estimating arterial delay and arterial dispersion (t , α , σ) values for outputting blood perfusion indices for a region of interest (ROI) by operating a computer program on intensity data in a computer comprising:

- a. applying a first gamma-variate function (GVF) to an arterial input function (AIF_a) to provide an estimated first model of a vascular transport function

$$h_a(t), \text{ wherein for } t < t_1, h_a(t) = 0 \text{ and for } t \geq t_1, h_a(t) = \frac{1}{\sigma_1} (t - t_1)^{\alpha_1} e^{-(t-t_1)/\sigma_1},$$

wherein an estimated t_1 is the transit time of a contrast agent from a measured initial said AIF_a to a region of interest (ROI);

- b. estimating an initial value σ_1 of said contrast agent, wherein said $\sigma_1 = (t_1)(\beta_1)/(1-\beta_1)$, wherein said β_1 is a known relative dispersion value having a range from 0 to 1;

- c. convolving $AIF_a(t)$ with said $h_a(t, \alpha_1=0)$ for obtaining an arterial input function $AIF_t(t) = AIF_a(t) \otimes h_a(t, \alpha_1=0)$ at said ROI;

- d. estimating a blood flow rate F_t and a tissue impulse residue function $R_e(t)$ by deconvolving a concentration curve $C(t) = (F_t/k_H)AIF_t(t) \otimes R_e(t)$, wherein k_H is a hemocrit correction constant having a known value; and

- e. outputting estimated and optimized tissue mean transit time and dispersion (t_2 , α_2 , σ_2) values from an estimated transport function $h_e(t)$ for input to a simulated transport function $h_s(t)$, wherein a simulated tissue impulse residue function $R_s(t)$ is determined, wherein a simulated concentration curve $C_s(t)$ is

fitted to said measured $C(t)$ and quantitative said blood perfusion indices are calculated.

54. (NEW) The method of claim 53, wherein said intensity data is generated by
5 administering a contrast agent to a body lumen of a body during a dynamic
imaging scan, wherein said body lumen comprises an artery or vein, wherein
an image response from said contrast agent is recorded to computer data
storage in a computer.

10 55. (NEW) The method of claim 53, wherein said $C(t)$ is a temporal concentration
of said contrast agent obtained from said intensity data, wherein said intensity
data comprises contrast images sequentially acquired from a region in a body,
whereby said contrast agent concentration is plotted versus time.

15 56. (NEW) The method of claim 53, wherein said AIF_a is based on a measured
early arrival contrast agent peak intensity from a feeding blood vessel to said
ROI.

20 57. (NEW) The method of claim 53, wherein said AIF_a is scaled upward according
to a venous input function (VIF), wherein said VIF is based on a measured late
arrival contrast agent peak intensity from a large vein draining from said ROI.

58. (NEW) The method of claim 53, wherein said estimated transit time t_1 is the

transit time of said contrast agent from a measured initial said AIF_a of said contrast agent C(t) in a body lumen to said ROI, wherein said t₁ is estimated from plots of said AIF_a versus time and said C(t) versus time.

5 59. (NEW) The method of claim 53, wherein said h_a(t) is calculated using said estimated transit time t₁ and said estimated dispersion value σ₁, wherein h_a(t, α₁=0) is plotted versus time.

10 60. (NEW) The method of claim 53, wherein said estimated transport function h_e(t) is calculated using the relation h_e(t) = - dR_e(t)/dt.

15 61. (NEW) The method of claim 53, wherein said tissue mean transit time and dispersion (t₂, α₂, σ₂) values are estimated from said estimated transport function h_e(t), wherein said t₂, said σ₂ and said α₂ are input to a simulated transport function h_s(t), wherein said h_s(t) is said second gamma-variate function.

20 62. (NEW) The method of claim 53, wherein said simulated tissue impulse resistive function R_s(t) is determined using the relation $R_s(t) = 1 - \int_0^t h_s(\tau) d\tau$.

63. (NEW) The method of claim 53, wherein said simulated concentration curve C_s(t) is determined using the relation C_s(t) = (F_i/k_H)AIF_i(t) ⊗ R_e(t) = (F_i/k_H)

$$\int_0^t \text{AIF}_i(t) R_i(t-\tau) d\tau.$$

64. (NEW) The method of claim 53, wherein said F_t , said t_1 , said σ_1 , said α_2 , said t_2 , said α_2 , and said σ_2 are optimized by a least squares method to fit said $C_s(t)$ to said $C(t)$.

65. (NEW) The method of claim 53, wherein said perfusion indices have the relations:

- a. blood flow (BF) = F_t ;
- b. Mean Transit Time (MTT) = $t_2 + \sigma_2(1+\alpha_2)$;
- c. Blood Volume (BV) = BF * MTT;
- d. Arterial Delay (DT) = $t_1 + \sigma_1(1+\alpha_1)$;
- e. Arterial Dispersion time (ADT) = $\sigma_1 \sqrt{1 + \alpha_1}$;
- f. Tissue Dispersion Time (TDT) = $\sigma_2 \sqrt{1 + \alpha_2}$;
- g. Relative Arterial Dispersion (RAD) = ADT/DT; and
- h. Relative Tissue Dispersion (RTD) = TDT/MTT.

66. (NEW) The method of claim 53, wherein said $\text{AIF}_i(t)$ is measureable in a small lumen showing a delay relative to said $\text{AIF}_a(t)$, wherein optimized values for said σ_1 and said t_1 are determined by fitting said simulated $\text{AIF}_i(t)$ to said measured $\text{AIF}_i(t)$, wherein said relative dispersion β_1 is determined and applied to all other said intensity data of said ROI using said β_1 , wherein a more robust

fitting process is provided by a reduced number of parameters for optimization.

67. (NEW) The method of claim 66, wherein when said relative dispersion β_1 is determined, said vascular transport function $h_a(t)$ is described by a single variable said t_1 with a constant said β_1 , wherein a two-step method is used to determine said delay and said dispersion values comprising:

- a. deriving an initial tissue impulse residue function $R_0(t)$ by deconvolving $C(t) = (F_0/k_H)AIF_a(t) \otimes R_0(t)$ using a model-free singular value decomposition (SVD) method, wherein said time delay t_1 is determined by a maximum position of said $R_0(t)$ at $R_{0\max}(t=t_1)$; and
- b. determine said $AIF_t(t)$ at an input of said ROI using said $h_a(t)$ with said t_1 and said β_1 held constant, wherein said σ_1 is determined.

68. (NEW) The method of claim 67, wherein a value of tissue blood flow F_t and a corrected impulse residue function $R_e(t)$ are obtained by deconvolving $C(t) = (F_t/k_H)AIF_t(t) \otimes R_e(t)$ using said SVD method, wherein said perfusion indices are determined from a curve of said $R_e(t)$, wherein $MTT = \int_0^\infty R_e(\tau) d\tau$, $BF = F_t$, and $BV = BF * MTT$.

69. (NEW) The method of claim 53, wherein said contrast agent is in a tissue ROI having a tissue mean transit time τ , wherein a tissue impulse residue function is approximated by the relation $R(t > \tau) = Ee^{-k(t-\tau)}$ and $R(t \leq \tau) = 1$, wherein E is an extraction fraction of said contrast agent in said tissue, wherein k is a constant

clearance rate of said contrast agent diffusing from said tissue having a relation $k = E \cdot F_t / V_e$, wherein V_e is the volume fraction of extravascular and extracellular space (EES) in said tissue.

- 5 70. (NEW) The method of claim 69, wherein said tissue impulse residue function $R_s(t)$ of said simulated concentration curve $C_s(t)$ is replaced by an average impulse residue function that incorporates said contrast agent leaked out of a blood vessel into said tissue and gradually clearing from said tissue, wherein said simulated concentration curve $C_s(t)$ is fitted to said
- 10 measured $C(t)$ and quantitative said blood perfusion indices are calculated, wherein said E and said V_e are additional parameters optimized with other adjustable parameters using a least squares method.